Author’s Response
On the roles of skin type and sun exposure in the risk of endometriosis and melanoma
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In a previous issue of the International Journal of Epidemiology,1 we described significant associations between some cutaneous phenotypic traits associated with melanoma risk and the risk of endometriosis among participants of the French E3N cohort. Dr Grant argues that these findings can be explained by a low vitamin D level in women with these phenotypic traits.

First, Dr Grant’s statement that those with dark skin had higher risk of endometriosis in our study is based on an estimate that is not statistically significant and of low magnitude [odds ratio (OR) = 1.16, 95% confidence interval (CI) = 0.91–1.49], so no argument can be based on that finding.

Secondly, Dr Grant’s demonstration of a suspected causal association between endometriosis and low vitamin D levels is mostly indirect, based on (i) a known association between endometriosis and ovarian cancer—which has been attributed to chronic inflammation,2 and (ii) a potential association between ovarian cancer and vitamin D. Although ecological studies suggested an association between vitamin D and reduced risk of ovarian cancer, epidemiological studies did not confirm this association with serum levels of vitamin D3 or dietary vitamin D intakes,4 and investigations of VDR polymorphisms in relation to ovarian cancer have yielded inconsistent results.5–7 The basis of Dr Grant’s argument that endometriosis is associated with vitamin D because ovarian cancer may be linked to vitamin D is thus unreliable. Then, to our knowledge, there is no direct evidence that low concentration of 25-hydroxyvitamin-D3 [25(OH)D] is a risk factor for endometriosis. To date, few studies examined the relationship between vitamin D and risk of endometriosis, and more research is needed at this stage before any firm conclusions can be drawn. In fact, two reports actually suggested higher serum levels of 25(OH)D8 or 1.25-dihydroxyvitamin-D39 in endometriosis patients compared with controls, and another study found no significant difference in serum 25(OH)D levels between patients and controls.10

Thirdly, Dr Grant argues that individuals with high-risk phenotypes with regard to melanoma (such as fair skin, high skin sensitivity to the sun, high freckling density and high naevus counts) would tend to avoid the sun and thus have lower levels of vitamin D. This argument is speculative and is not supported by the literature. Indeed, it has been shown that the relationships between skin cancer awareness, individual risk and attitudes and behaviours towards sun exposure are complex, and that people with more sensitive skin do not necessarily avoid the sun.11 Moreover, individual levels of serum vitamin D depend on complex combinations of sun exposure, skin complexion and oral intake of vitamin D,12 and thus cannot be predicted on the basis of complexion only. Also, in a recent meta-regression analysis, Caucasians have been shown to have higher vitamin D levels than non-Caucasians.13 Finally, Dr Grant argues that naevus count is related to sun exposure in childhood. We agree that this factor is an important determinant of naevus density; however, naevi are mostly genetically determined.14,15 Also, his argument that individuals with naevi would not expose themselves to the sun at an adult age is speculative, unsubstantiated by any references.

Thus, although it is clearly of interest to better understand the relationship between several chronic conditions and vitamin D, there is no strong or consistent evidence for attributing our findings to low sun exposure and low vitamin D levels. Considering that similar genetic factors have been suggested to play a role in the aetiology of both endometriosis16–18 and melanoma,19–21 especially for CDKN2A, which has been associated with naevi,22 we believe that our hypothesis of common genetic features between endometriosis and melanoma warrants further investigation. Hence, because it is still unclear whether genes, hormones, environment or complex associations between these factors mostly explain our findings, further research is needed to elucidate common pathways between endometriosis and melanoma.
Is education causal? Yes

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In a provocative analysis piece Deary and Johnson critique the lack of theory behind the use of education as an explanatory variable in epidemiology.1 There are of course several well-defined sociological theories of education in relation to health, although it is a fair comment that these are not always sufficiently